FDA Public Hearing: Reporting of Adverse Events to Institutional Review Boards

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CIOMS VI Working Group Proposals

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What is CIOMS?

Council for

International

Organizations of

Medical

Sciences

www.cioms.ch

CIOMS Drug Safety Working Groups

CIOMS I	*International Reporting of Adverse Drug Reactions (1990*) Basis for ICH E2A (pre-approval reporting) and ICH E2B (electronic case submission of ICSRs)
CIOMS II	*International Reporting of Periodic Drug-Safety Update Summaries (1992)* Basis for ICH E2C (PSUR)
CIOMS III	*Guidelines for Preparing Company Core Clinical-Safety Information (1995)*
CIOMS III/V	CIOMS III Second Edition. Includes DCSI (1999)
CIOMS IV	*Benefit- Risk Balance for Marketed Drugs: Evaluating Safety Signals (1998)*
CIOMS V	*Current Challenges in Pharmacovigilance: Pragmatic Approaches (2001)*
CIOMS VI	"Managing Safety Information from Clinical Trials" (in press, 2005)

Other ongoing CIOMS initiatives (MedDRA, pharmacogenetics, ethics, ….)

Members of CIOMS WG VI

- AMANT, Argentina
- BfArM, Germany
- EMEA, London
- FDA, USA
- Health Canada
- Inst. Pasteur, Morocco
- MCA, UK
- MoH, Croatia
- MHLW, Japan
- TGA, Australia
- WHO, Switzerland
- AstraZeneca
- Aventis Pharma S.A.
- Bayer AG
- Cephalon Inc
- Eisai Co. Ltd.
- Eli Lilly & Co.
- F. Hoffman-LaRoche Ltd
- GlaxoSmithKline
- Merck & Co. Inc.
- Novartis Pharma AG
- Pfizer Inc
- Wyeth

CIOMS VI
Management of Safety Information from Clinical Trials

- Ethical Considerations
- Systematic Approach
- Data Collection
- Evaluation of Risk
- Statistical Analysis
- Regulatory Reporting and Other Communication of Safety Information from Clinical Trials (Chapter 7)

CIOMS VI
Reporting/Communication of Safety Information from Clinical Trials: Issues

- Expanding scope and size of development programs
- Increasing volume of AE reports can be overwhelming for investigators and IRBs
- Individual case reports do not always (and often do not) include important new safety information
- Important new information, best derived from evaluation of cases in aggregate, may not be effectively conveyed through sporadic case reporting

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

- *The CIOMS VI Working Group recommends replacing the current practice of sending large numbers of individual case reports to investigators and ethics committees with a more reasonable approach to communicating important safety information to all who need to know. Such an approach would involve periodic and* ad hoc *communications to investigators and ethics committees that include an update of important safety information as well as the evolving benefit-risk profile.*

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

- For unapproved products
  - Line listing of unblinded clinical trial cases that were expedited to regulatory authorities since the last report
  - Copy of the current development core safety information (DCSI) along with an explanation of any changes
  - Brief summary of the emerging safety profile
  - Quarterly updates, more or less depending on circumstances

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

- For approved products
  - Timeframe would depend on the extent to which new indications are being developed
  - For a product undergoing Phase III trials, continuation of the quarterly reports would be advisable
  - For well-established products, less frequent updates would be appropriate
  - At some point, there should only be a need to update investigators and IRBs when there is significant new information to report

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

- Line listings
  - Only unblinded expedited reports from clinical trials
  - Interval data, i.e., only cases expedited since the last update
  - Summary of the emerging safety profile should take into account all of the accumulating data
  - MedDRA preferred terms
  - Line listings generally should not include spontaneous reports; instead, significant issues arising from spontaneous reports can be described in narrative form in the update.

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

- *For Phase IV investigators and their associated IRBs, communication of changes to the Company Core Safety Information (CCSI) for the marketed product should be sufficient and periodic reports or line listings should no longer be necessary.*

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

- *If a significant safety issue is identified, either from an individual case report or review of aggregate data, then the sponsor should issue a prompt notification to all parties, namely regulatory authorities, investigators and IRBs.*

- *A significant safety issue could be defined as one that has a significant impact on the course of the clinical trial or program (including the potential for suspension of the trial programme or amendments to protocols) or warrants immediate update of informed consent.*

CIOMS VI Proposals Reporting/Communication of Safety Information to Investigators and IRBs

Result: A More Effective System

- Managing safety information from clinical trials
- Identifying and communicating important new safety information to all who need to be informed and to take action

Thank You for Your Attention